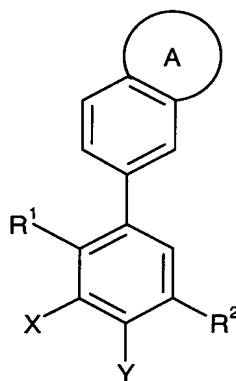


Amendments to the claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 (original). A compound of formula (I):



(I)

wherein

A is a fused 5-membered heteroaryl ring optionally substituted by up to two substituents independently selected from C₁₋₆alkyl, -(CH₂)_m-C₃₋₇cycloalkyl, halogen, cyano, trifluoromethyl, -(CH₂)_mOR³, -(CH₂)_mCO₂R³, -(CH₂)_mNR³R⁴, -(CH₂)_mCONR³R⁴, -(CH₂)_mNHCOR³, -(CH₂)_mSO₂NR³R⁴, -(CH₂)_mNHSO₂R³, -(CH₂)_mSO₂(CH₂)_nR⁵, a 5- or 6-membered heterocyclyl ring containing nitrogen optionally substituted by C₁₋₂alkyl or -(CH₂)_mCO₂R³, and a 5-membered heteroaryl ring optionally substituted by C₁₋₂alkyl;

R¹ is selected from methyl and chloro;

R² is selected from -NH-CO-R⁶ and -CO-NH-(CH₂)_q-R⁷;

R³ is selected from hydrogen, C₁₋₆alkyl optionally substituted by up to two OH groups, -(CH₂)_m-C₃₋₇cycloalkyl, -(CH₂)_mphenyl optionally substituted by R⁸ and/or R⁹ and -(CH₂)_mheteroaryl optionally substituted by R⁸ and/or R⁹,

R⁴ is selected from hydrogen and C₁₋₆alkyl, or

R³ and R⁴, together with the nitrogen atom to which they are bound, form a 5- or 6-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁰;

R⁵ is selected from C₁₋₆alkyl optionally substituted by up to three halogen atoms, C₂₋₆alkenyl optionally substituted by phenyl, C₃₋₇cycloalkyl, heteroaryl optionally substituted by up to three R⁸ and/or R⁹ groups, and phenyl optionally substituted by R⁸ and/or R⁹;

R⁶ is selected from hydrogen, C₁₋₆alkyl, -(CH₂)_q-C₃₋₇cycloalkyl, trifluoromethyl, -(CH₂)_rheteroaryl optionally substituted by R¹¹ and/or R¹², and -(CH₂)_rphenyl optionally substituted by R¹¹ and/or R¹²;

R⁷ is selected from hydrogen, C₁₋₆alkyl, C₃₋₇cycloalkyl, -CONHR¹³, phenyl optionally substituted by R¹¹ and/or R¹², and heteroaryl optionally substituted by R¹¹ and/or R¹²;

R⁸ and R⁹ are each independently selected from halogen, cyano, trifluoromethyl, nitro, C₁₋₆alkyl, C₁₋₆alkoxy, -CONR¹³R¹⁴, -COR¹⁵, -CO₂R¹⁵, and heteroaryl, or

R⁸ and R⁹ are linked to form a fused 5-membered heterocyclyl ring containing one heteroatom selected from oxygen, sulphur and N-R¹⁰, or a fused heteroaryl ring;

R¹⁰ is selected from hydrogen and methyl;

R¹¹ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_q-C₃₋₇cycloalkyl, -CONR¹³R¹⁴, -NHCOR¹⁴, halogen, CN, -(CH₂)_sNR¹⁶R¹⁷, trifluoromethyl, phenyl optionally substituted by one or more R¹² groups, and heteroaryl optionally substituted by one or more R¹² groups;

R¹² is selected from C₁₋₆alkyl, C₁₋₆alkoxy, halogen, trifluoromethyl, and -(CH₂)_sNR¹⁶R¹⁷;

R¹³ and R¹⁴ are each independently selected from hydrogen and C₁₋₆alkyl, or

R¹³ and R¹⁴, together with the nitrogen atom to which they are bound, form a 5- or 6-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁰, wherein the ring may be substituted by up to two C₁₋₆alkyl groups;

R¹⁵ is C₁₋₆alkyl;

R¹⁶ is selected from hydrogen, C₁₋₆alkyl and -(CH₂)_q-C₃₋₇cycloalkyl optionally substituted by C₁₋₆alkyl,

R¹⁷ is selected from hydrogen and C₁₋₆alkyl, or

R¹⁶ and R¹⁷, together with the nitrogen atom to which they are bound, form a 5- or 6-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁰;

X and Y are each independently selected from hydrogen, methyl and halogen;

m is selected from 0, 1, 2 and 3;

n is selected from 0, 1, 2 and 3;

q is selected from 0, 1 and 2;

r is selected from 0 and 1; and

s is selected from 0, 1, 2 and 3.

2 (original). A compound according to claim 1 wherein A is a fused 5-membered heteroaryl ring containing up to two heteroatoms independently selected from oxygen and nitrogen optionally substituted by up to two substituents independently selected from C₁₋₄alkyl, -(CH₂)_m-C₃₋₇cycloalkyl, -(CH₂)_mCO₂R³, -(CH₂)_mNR³R⁴, -(CH₂)_mCONR³R⁴, -(CH₂)_mNHCOR³, -(CH₂)_mSO₂(CH₂)_nR⁵, and a 5- or 6-membered heterocyclyl ring containing nitrogen optionally substituted by C₁₋₂alkyl or -(CH₂)_mCO₂R³.

3 (currently amended). A compound according to claim 1 ~~or claim 2~~ wherein R¹ is methyl.

4 (currently amended). A compound according to claim 1 ~~any one of the preceding claims~~ wherein R^2 is $-\text{CO}-\text{NH}-(\text{CH}_2)_q-\text{R}^7$.

5 (currently amended). A compound according to claim 1 ~~any one of the preceding claims~~ wherein X is hydrogen or fluorine.

6 (currently amended). A compound according to claim 1 ~~as defined in any one of Examples 1 to 141~~ which is:

N-Cyclopropyl-4-methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)benzamide;

4-Methyl-N-(3-morpholin-4-ylphenyl)-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)benzamide;

N-[4-Methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)phenyl]-2-pyrrolidin-1-ylisonicotinamide;

N-[4-Methyl-3-(3-methyl-1,2-benzisoxazol-6-yl)phenyl]-2-pyrrolidin-1-ylisonicotinamide; (GW 817258X)

N-[4-Methyl-3-(3-methyl-1,2-benzisoxazol-6-yl)phenyl]thiophene-3-carboxamide;

N-[4-Methyl-3-(3-methyl-1,2-benzisoxazol-6-yl)phenyl]-3-furamide;

4-Methyl-3-(3-methyl-1,2-benzisoxazol-6-yl)-N-(3-morpholin-4-ylphenyl)benzamide;

4-Methyl-3-(3-methyl-1,2-benzisoxazol-6-yl)-N-(1,3-thiazol-2-yl)benzamide;

N-Cyclopropyl-4-methyl-3-(3-methyl-1,2-benzisoxazol-6-yl)benzamide;

N-[4-Methyl-3-(3-methyl-1,2-benzisoxazol-5-yl)phenyl]-2-pyrrolidin-1-ylisonicotinamide;

N-Cyclopropyl-3-[3-({[2-hydroxy-1-(hydroxymethyl)ethyl]amino}methyl)-1,2-benzisoxazol-6-yl]-4-methylbenzamide;

N-(3-Methoxyphenyl)-4-methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)benzamide;

4-Methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)-N-(1,3,4-thiadiazol-2-yl)benzamide;

N-[4-Methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)phenyl]thiophene-3-carboxamide;

N-[4-Methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)phenyl]-3-furamide;

N-(Cyclopropylmethyl)-4-methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)benzamide;

N-Cyclopropyl-3-(1H-indazol-5-yl)-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-[1-(phenylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-{1-[(3-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

3-{1-[(3-Cyanophenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-4-methylbenzamide;

N-Cyclopropyl-3-{1-[(3,4-difluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

(GW 824473X)N-Cyclopropyl-4-methyl-3-[1-(methylsulfonyl)-1H-indazol-5-yl]benzamide (GW 825587X)

N-Cyclopropyl-3-[1-(2,3-dihydro-1-benzofuran-5-ylsulfonyl)-1H-indazol-5-yl]-4-methylbenzamide;

N-Cyclopropyl-3-{1-[(3-methoxyphenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

3-[1-(Benzylsulfonyl)-1H-indazol-5-yl]-N-cyclopropyl-4-methylbenzamide;

N-Cyclopropyl-3-{1-[(5-isoxazol-3-ylthien-2-yl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

3-{1-[(4-Acetylphenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-4-methylbenzamide;

Methyl 4-{[(5-{5-[(cyclopropylamino)carbonyl]-2-methylphenyl}-1H-indazol-1-yl)sulfonyl]methyl}benzoate; N-Cyclopropyl-3-{1-[(3,4-dimethoxyphenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-(1-{[4-(trifluoromethyl)phenyl]sulfonyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-{1-[(4-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

4-Methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)-N-(1,3-thiazol-2-yl)benzamide;

N-Cyclopropyl-4-methyl-3-[3-(1-piperazinyl)-1,2-benzisoxazol-6-yl]benzamide;

N-Cyclopropyl-4-methyl-3-[3-(4-morpholinyl)-1,2-benzisoxazol-6-yl]benzamide;
(GW 847638X)

N-Cyclopropyl-4-methyl-3-{3-[2-oxo-2-(1-piperazinyl)ethyl]-1,2-benzisoxazol-6-yl}benzamide; (GW 838902X)

Methyl (6-{5-[(cyclopropylamino)carbonyl]-2-methylphenyl}-1,2-benzisoxazol-3-yl)acetate;

N-Cyclopropyl-3-(3-{2-[(2-hydroxyethyl)amino]-2-oxoethyl}-1,2-benzisoxazol-6-yl)-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{3-[2-oxo-2-(1-piperidinyl)ethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-4-methyl-3-{3-[2-(methylamino)-2-oxoethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-3-(3-{2-[(3-hydroxypropyl)amino]-2-oxoethyl}-1,2-benzisoxazol-6-yl)-4-methylbenzamide;

N-Cyclopropyl-3-(3-{2-[(cyclopropylmethyl)amino]-2-oxoethyl}-1,2-benzisoxazol-6-yl)-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-3-{3-[2-(ethylamino)-2-oxoethyl]-1,2-benzisoxazol-6-yl}-4-methylbenzamide;

N-Cyclopropyl-3-{3-[2-(cyclopropylamino)-2-oxoethyl]-1,2-benzisoxazol-6-yl}-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{3-[2-(4-morpholinyl)-2-oxoethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-4-methyl-3-{3-[2-({3-(methyloxy)phenyl}methyl)amino]-2-oxoethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-4-methyl-3-{3-[2-oxo-2-(1,3-thiazol-2-ylamino)ethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-4-methyl-3-{3-[(4-methyl-1-piperazinyl)methyl]-1,2-benzisoxazol-6-yl}benzamide;

N-Cyclopropyl-4-methyl-3-[3-(1-piperidinylmethyl)-1,2-benzisoxazol-6-yl]benzamide;

N-Cyclopropyl-4-methyl-3-[3-(4-morpholinylmethyl)-1,2-benzisoxazol-6-yl]benzamide;

N-Cyclopropyl-4-methyl-3-[3-(1-pyrrolidinylmethyl)-1,2-benzisoxazol-6-yl]benzamide;

3-(3-Amino-1,2-benzisoxazol-6-yl)-N-cyclopropyl-4-methylbenzamide;

N-Cyclopropyl-3-[3-(cyclopropylamino)-1,2-benzisoxazol-6-yl]-5-fluoro-4-methylbenzamide;

6-{5-[(Cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-N-(cyclopropylmethyl)-1,2-benzisoxazole-3-carboxamide;

6-{5-[(Cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-N-propyl-1,2-benzisoxazole-3-carboxamide;

6-{5-[(Cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-N-methyl-1,2-benzisoxazole-3-carboxamide;

6-{5-[(Cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-N,N-dimethyl-1,2-benzisoxazole-3-carboxamide;

N-Cyclopropyl-6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-1,2-benzisoxazole-3-carboxamide;

1,1-Dimethylethyl 5-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-1H-indazole-1-carboxylate;

N-Cyclopropyl-3-fluoro-5-(1H-indazol-5-yl)-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{1-[(1-methylethyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-[1-(ethylsulfonyl)-1H-indazol-5-yl]-4-methylbenzamide;

N-Cyclopropyl-3-[1-(cyclopropylsulfonyl)-1H-indazol-5-yl]-4-methylbenzamide;

Methyl 5-[(5-{5-[(cyclopropylamino)carbonyl]-2-methylphenyl}-1H-indazol-1-yl)sulfonyl]-2-furancarboxylate;

3-[1-(2,1,3-Benzoxadiazol-4-ylsulfonyl)-1H-indazol-5-yl]-N-cyclopropyl-4-methylbenzamide;

N-Cyclopropyl-3-{1-[(2-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{1-[(4-methylphenyl)sulfonyl]-1H-indazol-5-yl}benzamide; (GW 850903X)

N-Cyclopropyl-4-methyl-3-[1-(2-thienylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-{1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-[1-(propylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-4-methyl-3-{1-[(2-nitrophenyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-4-methyl-3-{1-[(2,2,2-trifluoroethyl)sulfonyl]-1H-indazol-5-yl}benzamide;

3-{1-[(2-Cyanophenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{1-[(1,3,5-trimethyl-1H-pyrazol-4-yl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-4-methyl-3-{1-[(1-methyl-1H-imidazol-4-yl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(2-thienylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(3-thienylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[(4-methylphenyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(1-{[4-(methyloxy)phenyl]sulfonyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(1-{[4-(1-methylethyl)phenyl]sulfonyl}-1H-indazol-5-yl)benzamide;

3-{1-[4-Chlorophenyl]sulfonyl}-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-{1-[2,4-difluorophenyl]sulfonyl}-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

3-{1-[3-Chlorophenyl]sulfonyl}-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-5-{1-[5-fluoro-2-methylphenyl]sulfonyl}-1H-indazol-5-yl}-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-5-{1-[3-fluorophenyl]sulfonyl}-1H-indazol-5-yl}-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(1-{[3-(methyloxy)phenyl]sulfonyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-{1-[3,5-difluorophenyl]sulfonyl}-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[3-methylphenyl]sulfonyl}-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[1-methylethyl]sulfonyl}-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(propylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(methylsulfonyl)-1H-indazol-5-yl]benzamide;

3-[1-(Butylsulfonyl)-1H-indazol-5-yl]-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(octylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-[1-(cyclopropylsulfonyl)-1H-indazol-5-yl]-5-fluoro-4-methylbenzamide;

3-{1-[(5-Chloro-2-thienyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-{1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-{1-[(1,2-dimethyl-1H-imidazol-4-yl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-[1-(ethylsulfonyl)-1H-indazol-5-yl]-5-fluoro-4-methylbenzamide;

3-{1-[(2-Chlorophenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[(2-methylphenyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-{1-[(4-ethylphenyl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[(4-propylphenyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-{1-[(3,4-difluorophenyl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

3-{1-[(4-Butylphenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(phenylsulfonyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[(phenylmethyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(1-[(E)-2-phenylethenyl]sulfonyl)-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-{1-[(2,5-difluorophenyl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-5-{1-[(2-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

3-{1-[(4-Cyanophenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-[1-(2,3-dihydro-1-benzofuran-5-ylsulfonyl)-1H-indazol-5-yl]-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[(4-methylphenyl)sulfonyl]-1H-indol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(phenylsulfonyl)-1H-indol-5-yl]benzamide;

N-Cyclopropyl-3-[1-(cyclopropylmethyl)-1H-indazol-5-yl]-4-methylbenzamide;

1,1-Dimethylethyl 4-(5-{5-[(cyclopropylamino)carbonyl]-2-methylphenyl}-1H-indazol-1-yl)-1-piperidinecarboxylate;

N-Cyclopropyl-4-methyl-3-[1-(4-piperidinyl)-1H-indazol-5-yl]benzamide hydrochloride;

Methyl (5-{5-[(cyclopropylamino)carbonyl]-2-methylphenyl}-1H-indazol-1-yl)acetate;

N-Cyclopropyl-3-(1H-indazol-6-yl)-4-methylbenzamide;

N-Cyclopropyl-3-{3-[(4-fluorophenyl)sulfonyl]-1H-indazol-6-yl}-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[3-(methylsulfonyl)-1H-indazol-6-yl]benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(3-methyl-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[3-methyl-1-(2-thienylsulfonyl)-1H-indazol-5-yl]benzamide; (GSK239043A)

Methyl (5-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-1H-indazol-1-yl)acetate; (GSK251057A)

N-Cyclopropyl-4-methyl-3-{1-[2-({[4-(methyloxy)phenyl]methyl}amino)-2-oxoethyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-4-methyl-3-(1-{2-oxo-2-[(phenylmethyl)amino]ethyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-4-methyl-3-[1-(2-{[(4-methylphenyl)methyl]amino}-2-oxoethyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-4-methyl-3-(1-{2-[(4-{(methylamino)carbonyl}phenyl)methyl]amino}-2-oxoethyl)-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-4-methyl-3-{1-[2-oxo-2-(propylamino)ethyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-(1-{2-[(cyclopropylmethyl)amino]-2-oxoethyl}-1H-indazol-5-yl)-4-methylbenzamide;

N-Cyclopropyl-3-(1-{2-[(2,2-dimethylpropyl)amino]-2-oxoethyl}-1H-indazol-5-yl)-4-methylbenzamide;

N-Cyclopropyl-4-methyl-3-{1-[2-(4-morpholinyl)-2-oxoethyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(1-{2-oxo-2-[(phenylmethyl)amino]ethyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-[1-(2-{[(4-methylphenyl)methyl]amino}-2-oxoethyl)-1H-indazol-5-yl]benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[2-({[4-(methyloxy)phenyl]methyl}amino)-2-oxoethyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-(1-{2-[(4-{(methylamino)carbonyl}phenyl)methyl]amino]-2-oxoethyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[2-oxo-2-(propylamino)ethyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-3-(1-{2-[(cyclopropylmethyl)amino]-2-oxoethyl}-1H-indazol-5-yl)-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-fluoro-4-methyl-5-{1-[2-(4-morpholinyl)-2-oxoethyl]-1H-indazol-5-yl}benzamide;

N-Cyclopropyl-4-methyl-3-(1-{2-[(1-methylethyl)amino]-2-oxoethyl}-1H-indazol-5-yl)benzamide;

N-Cyclopropyl-3-(1-{2-[(2,2-dimethylpropyl)amino]-2-oxoethyl}-1H-indazol-5-yl)-5-fluoro-4-methylbenzamide;

N-Cyclopropyl-3-{2-[(cyclopropylcarbonyl)amino]-1,3-benzothiazol-6-yl}-4-methylbenzamide; or a pharmaceutically acceptable salt thereof.

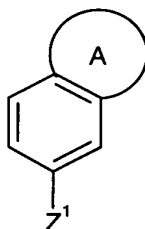
7 (currently amended). A pharmaceutical composition comprising a compound according to claim 1 as claimed in any one of claims 1 to 6 in admixture with one or more pharmaceutically acceptable carriers, diluents or excipients.

8 (currently amended). A method for treating a condition or disease state mediated by p38 kinase activity in a patient in need thereof or mediated by cytokines produced by the activity of p38 kinase comprising administering to a patient in need a compound thereof as claimed in any one of claims 1 to 6 said patient a compound according to claim 1.

9 (currently amended). A method for treating Use of a compound as claimed in any one of claims 1 to 6 in the manufacture of a medicament for use in the treatment of a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase in a patient in need thereof, comprising administering to said patient an effective amount of a compound according to claim 1.

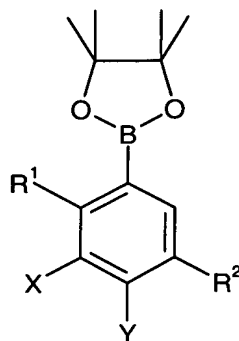
10 (currently amended). A process for preparing a compound of formula (I) as ~~claimed in any one of claims 1 to 6~~ according to claim 1 which comprises

(a) reacting a compound of formula (II)

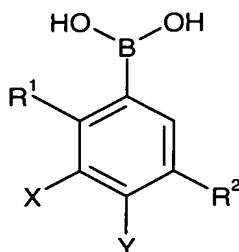


(II)

in which A is defined in claim 1 and Z¹ is halogen,
with a compound of formula (IIIA) or (IIIB)



(III A)

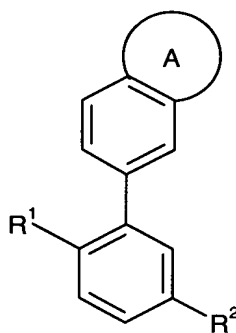


(III B)

in which R^1 , R^2 , X and Y are as defined in claim 1,
 in the presence of a catalyst, or

(b) final stage modification of one compound of formula (I) as defined in claim 1
 to give another compound of formula (I) as defined in claim 1.

11 (original). A compound of formula (IA):



(IA)

wherein

A is a fused 5-membered heteroaryl ring optionally substituted by up to two substituents independently selected from C_{1-6} alkyl, $-(CH_2)_m-C_{3-7}$ cycloalkyl, halogen, cyano, trifluoromethyl, $-(CH_2)_mOR^3$, $-(CH_2)_mNR^3R^4$, $-(CH_2)_mCONR^3R^4$, $-(CH_2)_mNHCOR^3$, $-(CH_2)_mSO_2NR^3R^4$, $-(CH_2)_mNHSO_2R^3$, $-(CH_2)_mSO_2(CH_2)_nR^5$, a 5- or 6-membered heterocyclyl ring containing nitrogen

optionally substituted by C₁₋₂alkyl and a 5-membered heteroaryl ring optionally substituted by C₁₋₂alkyl;

R¹ is selected from methyl and chloro;

R² is selected from -NH-CO-R⁶ and -CO-NH-(CH₂)_q-R⁷;

R³ is selected from hydrogen, C₁₋₆alkyl optionally substituted by up to two OH groups, -(CH₂)_m-C₃₋₇cycloalkyl, -(CH₂)_mphenyl optionally substituted by R⁸ and/or R⁹ and -(CH₂)_mheteroaryl optionally substituted by R⁸ and/or R⁹

R⁴ is selected from hydrogen and C₁₋₆alkyl, or

R³ and R⁴, together with the nitrogen atom to which they are bound, form a 5- or 6-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁰;

R⁵ is selected from C₁₋₆alkyl, C₃₋₇cycloalkyl, heteroaryl optionally substituted by R⁸ and/or R⁹, and phenyl optionally substituted by R⁸ and/or R⁹;

R⁶ is selected from hydrogen, C₁₋₆alkyl, -(CH₂)_q-C₃₋₇cycloalkyl, trifluoromethyl, -(CH₂)_rheteroaryl optionally substituted by R¹¹ and/or R¹², and -(CH₂)_rphenyl optionally substituted by R¹¹ and/or R¹²;

R⁷ is selected from hydrogen, C₁₋₆alkyl, C₃₋₇cycloalkyl, CONHR¹³, phenyl optionally substituted by R¹¹ and/or R¹², and heteroaryl optionally substituted by R¹¹ and/or R¹²;

R⁸ and R⁹ are each independently selected from halogen, cyano, trifluoromethyl, C₁₋₆alkyl, C₁₋₆alkoxy, COR¹⁵, CO₂R¹⁵, and heteroaryl, or

R⁸ and R⁹ are linked to form a fused 5-membered heterocyclyl ring containing one heteroatom selected from oxygen, sulphur and N-R¹⁰;

R¹⁰ is selected from hydrogen and methyl;

R¹¹ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_q-C₃₋₇cycloalkyl, -CONR¹³R¹⁴, -NHCOR¹⁴, halogen, CN, -(CH₂)_sNR¹⁶R¹⁷, trifluoromethyl, phenyl optionally substituted by one or more R¹² groups, and heteroaryl optionally substituted by one or more R¹² groups;

R¹² is selected from C₁₋₆alkyl, C₁₋₆alkoxy, halogen, trifluoromethyl, and -(CH₂)_sNR¹⁶R¹⁷;

R¹³ and R¹⁴ are each independently selected from hydrogen and C₁₋₆alkyl, or

R¹³ and R¹⁴, together with the nitrogen atom to which they are bound, form a 5- or 6-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁰, wherein the ring may be substituted by up to two C₁₋₆alkyl groups;

R¹⁵ is C₁₋₆alkyl;

R¹⁶ is selected from hydrogen, C₁₋₆alkyl and -(CH₂)_q-C₃₋₇cycloalkyl optionally substituted by C₁₋₆alkyl,

R¹⁷ is selected from hydrogen and C₁₋₆alkyl, or

R¹⁶ and R¹⁷, together with the nitrogen atom to which they are bound, form a 5- or 6-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁰;

m is selected from 0, 1, 2 and 3;

n is selected from 0, 1, 2 and 3;

q is selected from 0, 1 and 2;
r is selected from 0 and 1; and
s is selected from 0, 1, 2 and 3.

12 (new). A compound according to claim 1 which is:

N-[4-methyl-3-(3-piperidin-4-yl-1,2-benzisoxazol-6-yl)phenyl]-2-pyrrolidin-1-ylisonicotinamide;

N-cyclopropyl-4-methyl-3-[1-(phenylsulfonyl)-1H-indazol-5-yl]benzamide;

N-cyclopropyl-3-{1-[(3-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

N-cyclopropyl-4-methyl-3-[1-(methylsulfonyl)-1H-indazol-5-yl]benzamide;

N-cyclopropyl-3-{1-[(4-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

N-cyclopropyl-4-methyl-3-[3-(4-morpholinyl)-1,2-benzisoxazol-6-yl]benzamide;

N-cyclopropyl-4-methyl-3-{3-[2-oxo-2-(1,3-thiazol-2-ylamino)ethyl]-1,2-benzisoxazol-6-yl}benzamide;

N-cyclopropyl-4-methyl-3-[3-(4-morpholinylmethyl)-1,2-benzisoxazol-6-yl]benzamide;

N-cyclopropyl-4-methyl-3-[3-(1-pyrrolidinylmethyl)-1,2-benzisoxazol-6-yl]benzamide;

N-cyclopropyl-4-methyl-3-{1-[(1-methylethyl)sulfonyl]-1H-indazol-5-yl}benzamide);

N-cyclopropyl-3-[1-(ethylsulfonyl)-1H-indazol-5-yl]-4-methylbenzamide;

N-cyclopropyl-3-[1-(cyclopropylsulfonyl)-1H-indazol-5-yl]-4-methylbenzamide;

N-cyclopropyl-4-methyl-3-[1-(2-thienylsulfonyl)-1H-indazol-5-yl]benzamide;

3-{1-[(2-cyanophenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-4-methylbenzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-[1-(2-thienylsulfonyl)-1H-indazol-5-yl]benzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-[1-(3-thienylsulfonyl)-1H-indazol-5-yl]benzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-{1-[(1-methylethyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-[1-(propylsulfonyl)-1H-indazol-5-yl]benzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-[1-(methylsulfonyl)-1H-indazol-5-yl]benzamide;

3-[1-(butylsulfonyl)-1H-indazol-5-yl]-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-cyclopropyl-3-[1-(cyclopropylsulfonyl)-1H-indazol-5-yl]-5-fluoro-4-methylbenzamide;

3-{1-[(5-chloro-2-thienyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-cyclopropyl-3-{1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-cyclopropyl-3-[1-(ethylsulfonyl)-1H-indazol-5-yl]-5-fluoro-4-methylbenzamide;

3-{1-[(2-chlorophenyl)sulfonyl]-1H-indazol-5-yl}-N-cyclopropyl-5-fluoro-4-methylbenzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-{1-[(2-methylphenyl)sulfonyl]-1H-indazol-5-yl}benzamide;

N-cyclopropyl-3-fluoro-4-methyl-5-[1-(phenylsulfonyl)-1H-indazol-5-yl]benzamide;

N-cyclopropyl-3-{1-[(2,5-difluorophenyl)sulfonyl]-1H-indazol-5-yl}-5-fluoro-4-methylbenzamide;

N-cyclopropyl-3-fluoro-5-{1-[(2-fluorophenyl)sulfonyl]-1H-indazol-5-yl}-4-methylbenzamide;

N-cyclopropyl-3-[1-(cyclopropylmethyl)-1H-indazol-5-yl]-4-methylbenzamide; and

N-cyclopropyl-3-fluoro-4-methyl-5-[3-methyl-1-(2-thienylsulfonyl)-1H-indazol-5-yl]benzamide.